

Erythrocytosis **(Polycythemia)**

Dr Salwa Bakr Hassan

Ass. Prof. Laboratory Hematology

College of medicine

PNU

Objective

By the end of this lecture the students must be able to :

- Define & classify Polycythaemia.
- Causes of Polycythaemia
- Criteria to diagnose Polycythaemia vera (PV) .
- Clinical picture, laboratory finding, complication & treatment of PRV.

Polycythaemia

Polycythaemia (erythrocytosis) is defined as an increase in the haemoglobin concentration above the upper limit of normal for the patient's age and sex.

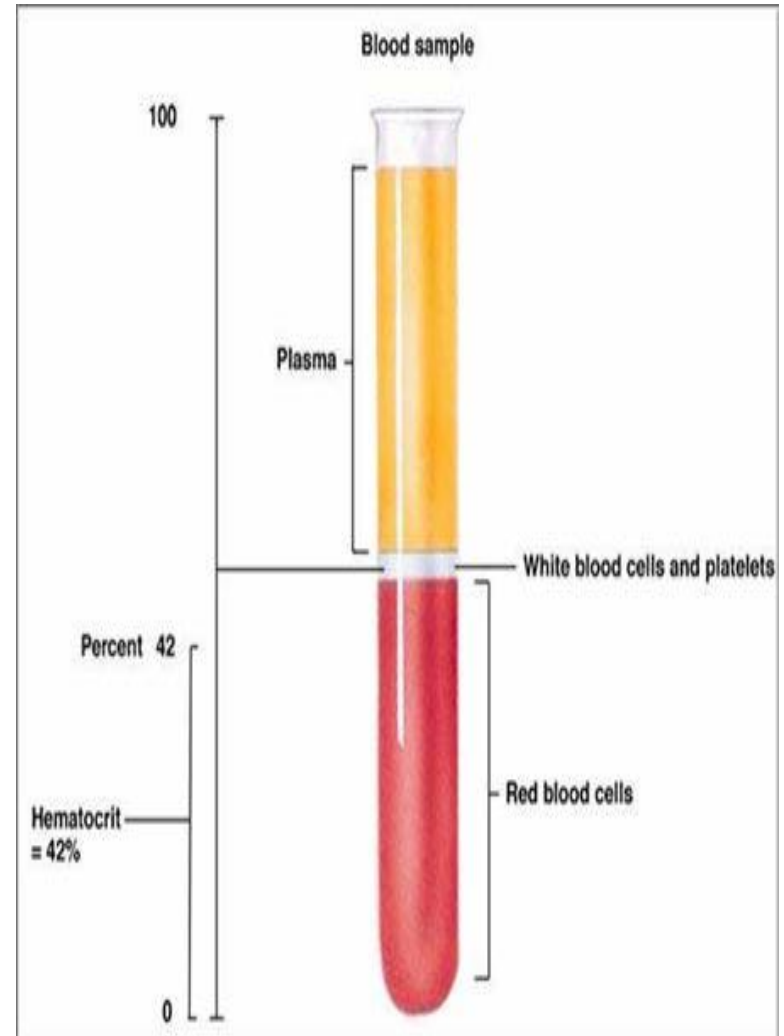
Definition of Erythrocytosis

- If HCT > 60% there will be increase in red cell mass.
- If Hb >18.5g/dl or HCT > 52% in men or
- Hb >16.5g/dl or HCT > 48% in women, indicate that erythrocytosis is likely but isotope studies is required

- Normal hematocrit :
 - Male 47 ± 5 percent
 - Female 42 ± 5 percent
- Normal hemoglobin :
 - Male 15 ± 2 gm/dl
 - Female 13.5 ± 1.5 gm/dl

Classification of polycythaemia

- **Relative (pseudo)vs Absolute**
- **Absolute erythrocytosis**
 - **Hct :**
male > 60%,
female > 55%



Erythrocytosis (Polycythemia)

I. Relative or spurious erythrocytosis

Relative polycythemia is an apparent rise of the erythrocyte level in the blood; however, the underlying cause is reduced blood plasma.

- Dehydration: water deprivation, vomiting
- Plasma loss: burns, enteropathy

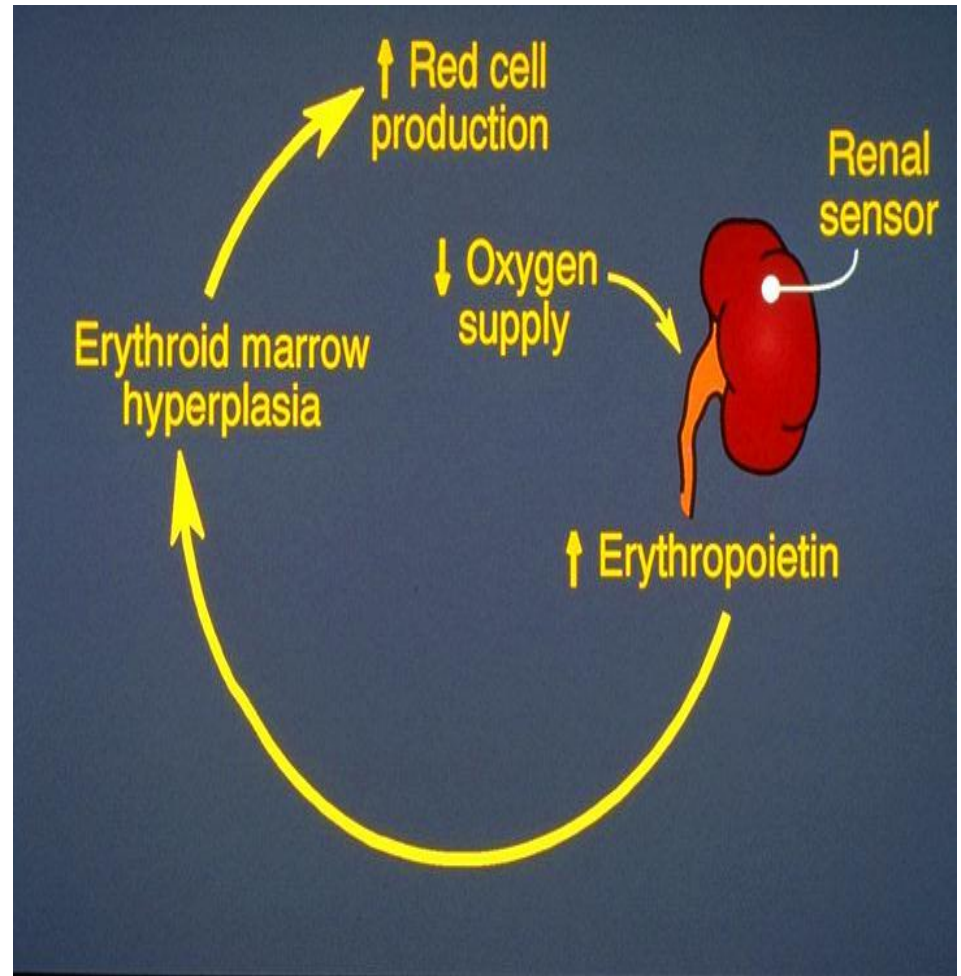
II. Absolute erythrocytosis

- Primary marrow diseases: **1^{ry}** erythrocytosis, PRV.
- Secondary : increased EPO production.

2ry Erythrocytosis

– **Reactive (Secondary)** : increased EPO production

- Tissue hypoxia
 - Lung diseases : COPD
 - Heart disease: Rt to Lt shunt
 - High altitude
 - Abnormal Hb,
 - smoking
- Tumors produce EPO
 - Hypernephroma
 - Hepatoma
- Renal diseases
 - Polycystic kidney
 - Renal artery stenosis



Polycythemia Vera (PV), **Acquired 1ry Polycythemia**

- Malignant clonal proliferation of hematopoietic stem cells leading to excessive erythrocyte production characterized as a panhyperplastic, malignant, and neoplastic marrow disorder.
- The increase in RBC mass occurs independent of erythropoietin.
- **Median age 60 years**
- **Mutation of Janus 2 kinase gene (*JAK2* V617F)**
- **Panmyelosis**

Pathogenesis

Thrombosis

- **High Hct**
- **Platelet**
 - No correlation with platelet count
 - Platelet functional defect
- **Abnormal in vivo activation of leukocyte, endothelial cell**
- **Decrease natural anticoagulant**
- **Decrease fibrinolytic activity**

P. Vera - Symptoms & Signs

- **Symptoms**

- Headache
- Weakness
- Pruritus
- Dizziness
- Visual disturbance
- Weight loss

- **Signs**

- Splenomegaly
- Skin plethora
- Hepatomegaly
- Conjunctival plethora
- Systolic hypertension
- Gout (↑uric acid)

Erythromelalgia

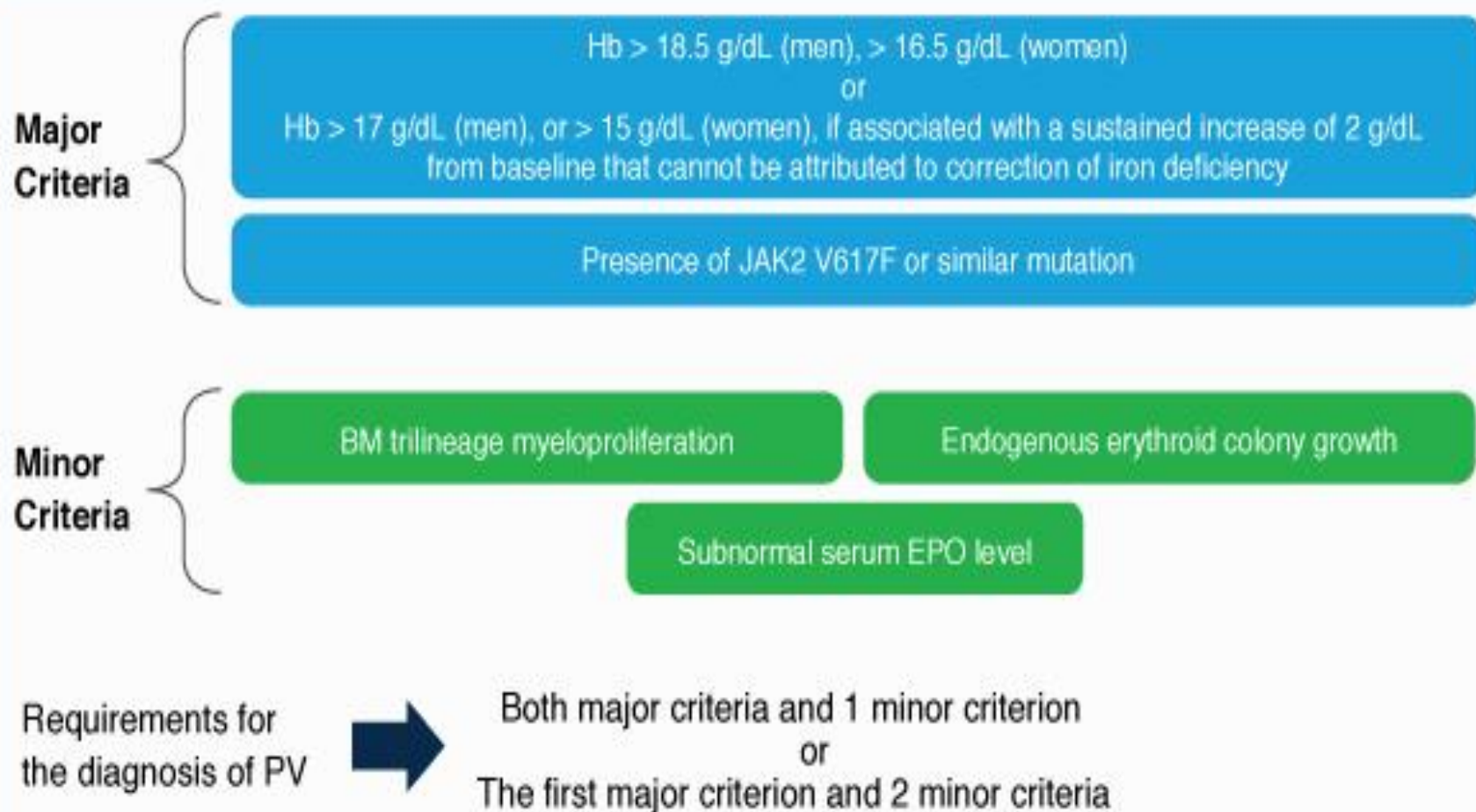


- Burning pain in the feet or hands accompanied by erythema, pallor, or cyanosis
- Microvascular thrombosis

Clue diagnosis PV

- High Hct, absent secondary erythrocytosis
- Headache, plethora, thrombosis, pruritus
- Mild to moderate splenomegaly
- Hepatomegaly
- Leukocytosis, thrombocytosis
- Panmyelosis
- Low erythropoietin level
- *JAK2* mutation

World Health Organization Criteria for Diagnosis of Polycythemia Vera — 2008³



BM, bone marrow; **EPO**, erythropoietin; **Hb**, hemoglobin; **LDH**, lactate dehydrogenase;
MF, myelofibrosis; **PV**, polycythemia vera.

Criteria for diagnosis of polycythaemia vera

(From Mc Mullin M.F. et al., 2007)

JAK2-positive polycythemia vera

- A1. High hematocrit (>0.52 in men, >0.48 in women)
or raised red cell mass (>25% above predicted)
 - A2. Mutation in JAK2
- Diagnosis require both criteria to be present*

JAK2-negative polycythemia vera

- A1. Raised red cell mass (>25% above predicted)
or hematocrit ≥ 0.60 in men, ≥ 0.56 in women
 - A2. Absence of a mutation in JAK2
 - A3. No case of secondary erythrocytosis
 - A4. Palpable splenomegaly
 - A5. Presence of an acquired genetic abnormality
(excluding BCR-ABL) in the hemotopoietic cells
 - B1. Thrombocytosis (platelet count $>450 \times 10^9/l$)
 - B2. Neutrophil leucocytosis (neutrophil count $>10 \times 10^9/l$
In non smokers, $>12.5 \times 10^9/l$ in smokers)
 - B3. Radiological evidence of splenomegaly
 - B4. Endogenous erythroid colonies or low serum erythropoietin
- Diagnosis requires A1 + A2 + A3 + either one other A or two B criteria
-

Laboratory

- **CBC**
- **Peripheral blood smear**
- **Bone marrow examination**
- **EPO level (normal or low)**
- ***JAK2* mutation**

CBC

Red cell

- Increase Hct, Hb
- Not increase in PV with iron deficiency

White cell

- Leukocytosis
- Band form, metamyelocyte, myelocyte (Lt shift)
- Increase basophil, eosinophil

Platelet

- Increase or normal

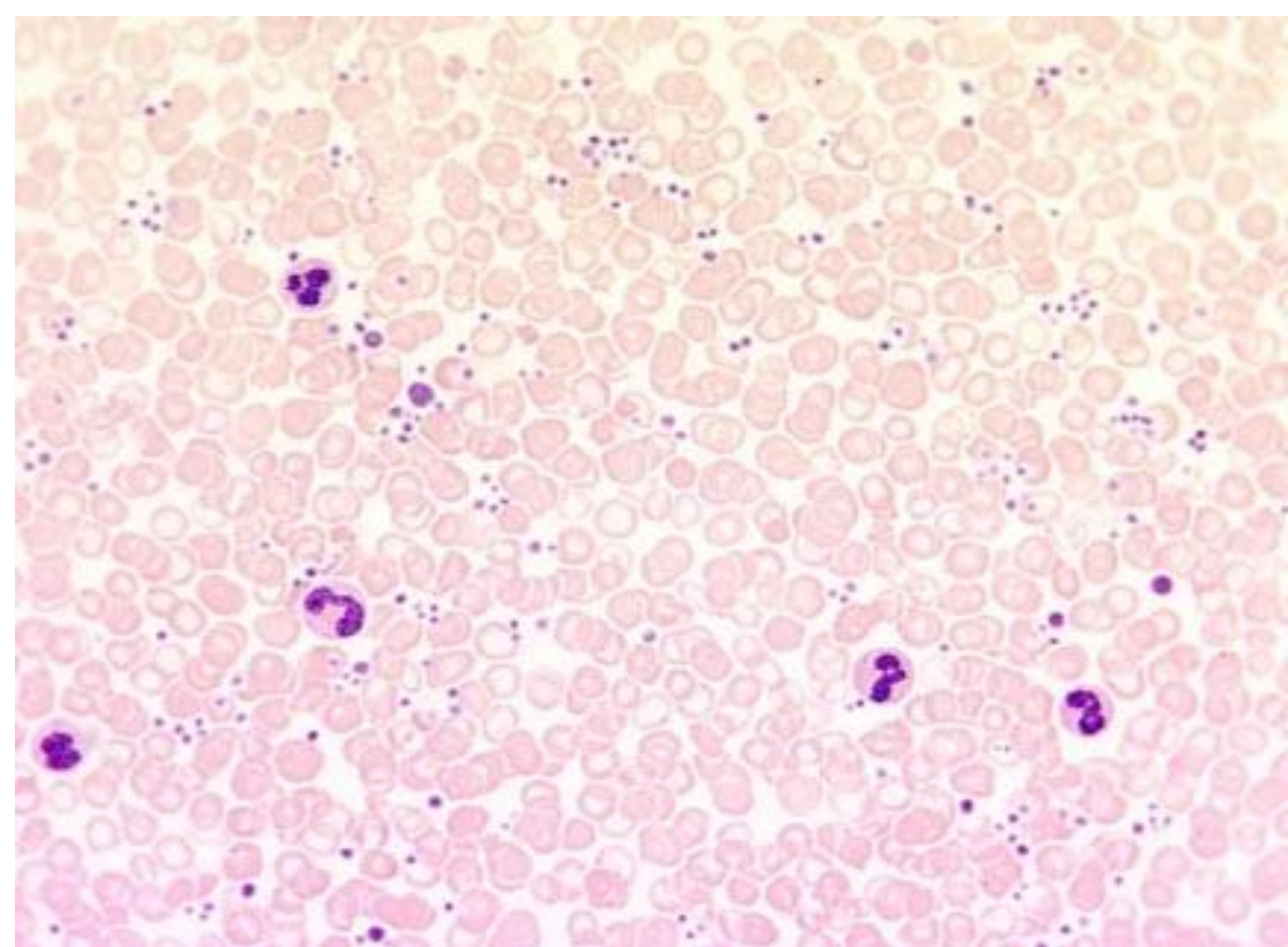
Blood smear

RBC: excess red cells, NC, NC

**hypochromic microcytic red
cells (iron deficiency)**

**WBC: increase with band form,
myelocyte ,metamyelocyte**

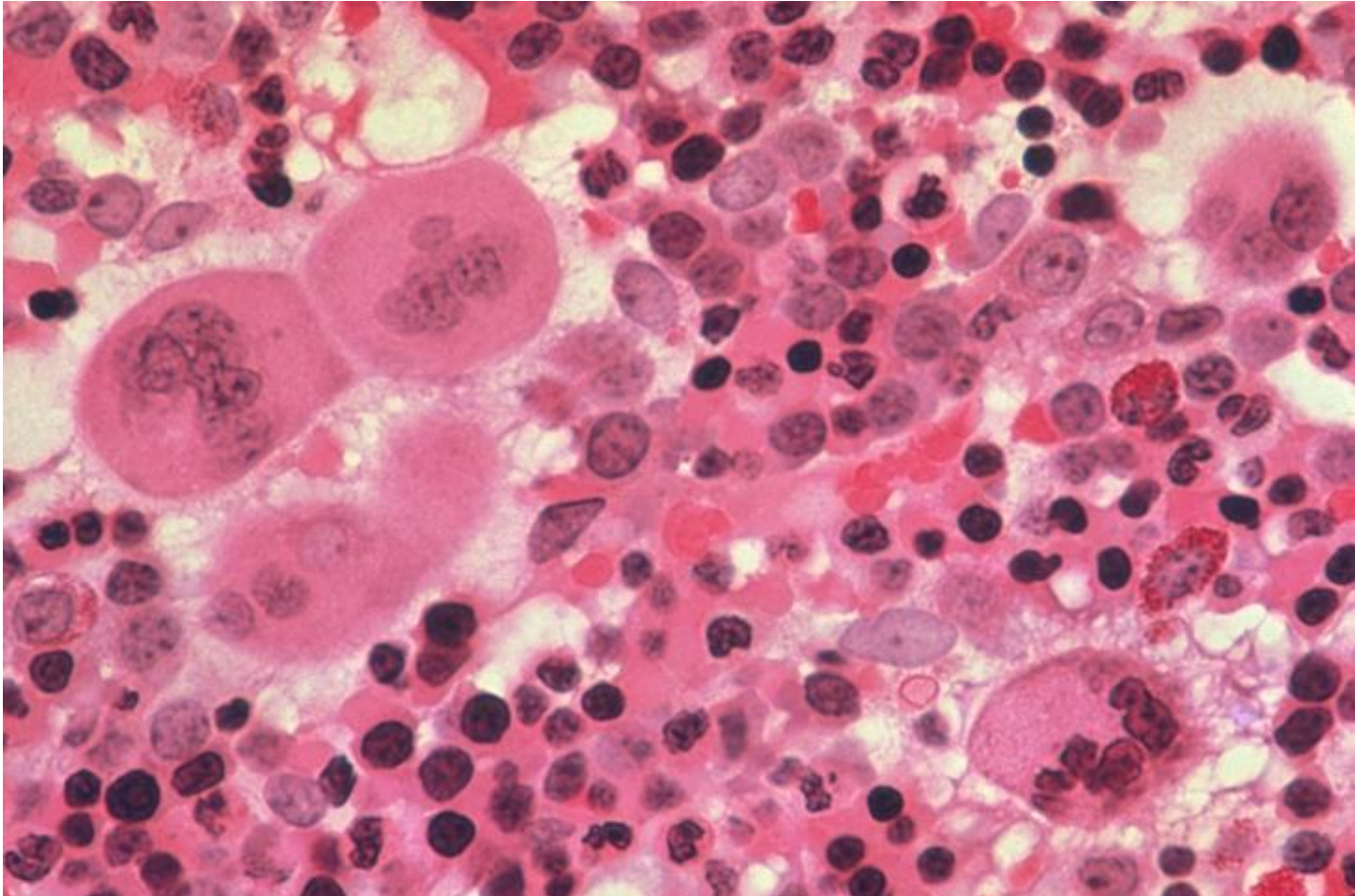
Platelet: increase



Bone marrow smear

- **Hypercellular marrow**
- **Increase erythroid, myeloid, megakaryocyte (panmyelosis)**
- **Normal maturation of myeloid series**
- **M:E = 2-3:1**
- **Increase megakaryocytes with different size**
- **Negative iron stain**

P. vera - Bone Marrow Biopsy



Cause of death

- **Cause of death**
 - **Thrombosis**
 - **Malignancy : acute leukemia, non-RE malignancy**
 - **Myelofibrosis**
 - **Bleeding**

Treatment Polycythemia Vera

Venesection to maintain
Hct < 45% male, <42% female

**Low dose
Aspirin**

high risk of thrombosis

- Age > 60 years
- Previous thrombosis
- Other cardiovascular risk

Platelet > 1,500,000 / μ m

Age < 50 yr

Interferon

Age 50-70 yr

Hydroxyurea

Age > 70 yr

**Busulphan or
³²P**